



REVIEW ARTICLE

**Extended Release Dosage Forms - Novel Drug Delivery System
Choudhari SJ*, Singh SR**

Dr. L. H. Hiranandani College of Pharmacy, Ulhasnagar, Maharashtra, India.

Manuscript No: IJPRS/V3/I2/00306, Received On: 11/06/2014, Accepted On: 22/06/2014

ABSTRACT

The oral route of drug delivery is typically considered the preferred and most patient-convenient means of drug administration. The advances in the formulation technology of modified release dosage form with extended release oral dosage form has been widely accepted approach as compared to conventional immediate release formulations of the same drug, over which it provides a prolong release of the drug over extended period of time there by giving the better patient compliance and enhanced bioavailability and resulting blood concentration-time profiles of drugs that otherwise suffer from few limitations. Extended release system are considered a wiser approach for the drugs with short half-lives and which require repeated dosing, they are easy to formulate and are irrespective of absorption process from gastrointestinal tract after oral administration.

KEYWORDS

Extended Release Dosage Forms, Half-life, Drug Delivery System

INTRODUCTION

For many years the conventional dosage forms are used to treat the acute or chronic disease. Even today these conventional dosage forms as primary pharmaceutical product in market. Eg. Tablet, Capsule, Creams, Paste, Suppositories, Emulsion etc. These conventional dosage form provide drug release for immediately and it causes fluctuation of drug level in blood. Therefore to maintain the drug concentrations within the therapeutically effective range need novel drug delivery system.

Novel drug delivery system (NDDS) is a system for delivery of drug other than conventional drug delivery system. Novel drug delivery companies have existed since the late 1960s to enhanced oral drug delivery. Recently several techniques are developed to controlled or sustained and target the drug release for

Particular site. There are great opportunities for companies investing in R&D for new, improved drug delivery system, allowing for improved therapeutic absorption and efficacy in patients¹. Oral drug delivery method is the most widely utilized routes for administration among all alternatives that have been explored for systemic delivery of drug via various pharmaceutical products of different dosage forms. Popularity of the route is the ease of administration.

Controlled release (C.R) pharmaceutical products have gradually gained medical acceptance and popularity. Regulatory approval for marketing and their pharmaceuticals superiority and clinical benefits over immediate release pharmaceutical products have been increasingly recognized. Modified release oral dosage forms have brought new lease of life into drugs that have lost market potential due to requirement of frequent dosing, dose related toxic effects and gastro intestinal disturbances².

*Address for Correspondence:

Choudhari S. J.

Dr. L. H. Hiranandani College of Pharmacy,
Maharashtra, India.

E-Mail Id: sjc5121990@gmail.com

Modified release dosage forms are drug delivery systems (DDS) which, *by virtue of formulation and product design*, provide drug release in a modified form *distinct from that of the conventional dosage forms*. Drug release can either be delayed or extended in nature.

Delayed Release

Usually enteric coated tablets or capsules designed to pass through the stomach unaltered to release their medication within the intestinal tract.

Extended Release

Designed to release their medication in *controlled manner*, at *pre-determined rate, duration and location* in the body to *achieve and maintain optimum therapeutic blood levels* of drug.

The US FDA defines ER dosage form as

One that allows a reduction in dosing frequency to that presented by a conventional dosage form such as a solution or an immediate release dosage forms³.

Modified release dosage forms are divided into three categories:

- **Delayed release dosage forms**
- **Extended release dosage forms**
 - Controlled release dosage forms
 - Sustained release dosage forms
- **Targeted release dosage forms**

Delayed Release Dosage Forms

Delayed release dosage form is the one that releases the active ingredient at some time other than promptly after administration.

A delayed release dosage form does not produce or maintain uniform drug blood levels within the therapeutic range but nonetheless, is more effective for patient compliance than conventional dosage forms.

Examples of delayed release systems include enteric-coated tablets where timed release is achieved by a barrier coating.

Extended Release Dosage Forms

A dosage form that allows at least a twofold reduction in dosage frequency as compared to that drug presented as an immediate release form. Eg: Controlled release, Sustained release.

Sustained Release

It includes any drug delivery system that achieves slow release of drugs over an extended period of time not particularly at a pre-determined rate.

Controlled Release

It includes any drug delivery system from which the drug is delivered at a predetermined rate over a long period.

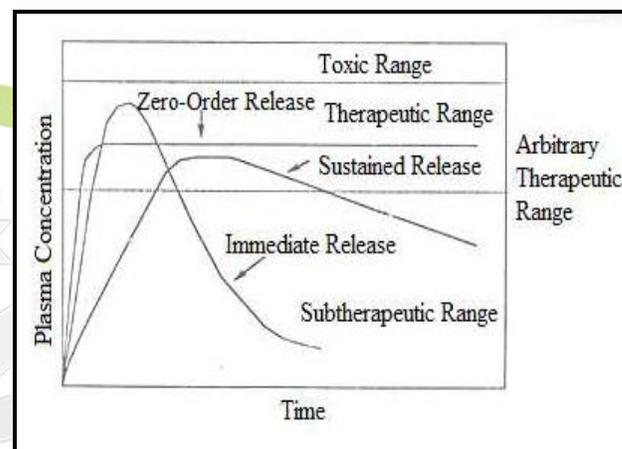


Figure 1.1: Plasma drug concentration profiles for conventional tablet formulation, a sustained release formulation and a zero order controlled release formulation

Targeted Release Dosage Forms

A dosage forms that releases drug at /near the intended physiological site of action. Targeted release dosage forms may have extended release characteristics^{1,4}.

Rationale for Extended Release Dosage Forms

- Drugs that are not inherently long lasting require multiple daily dosing to achieve the desired therapeutic effects.
- Multiple daily dosing is often inconvenient and can result in missed doses, made-up doses and patient non-compliant with therapeutic regimen.

- Blood levels of drugs from conventional immediate-release dosage forms taken more than once daily following definite schedule usually demonstrate sequential peaks and troughs (valleys) associated with each dose. Extended release tablets or capsules are commonly taken only once or twice daily compared with the conventional dosing of 2 to 4 times daily .
- Products are designed to provide **an immediate release of drug** which promptly produces the desired therapy, followed by gradual and continual release of additional amounts of drug to maintain this effect over a predetermined period of time.
- The need for night dosing of drugs may be eliminated³.

Advantages of Extended Release Dosage form Over Conventional Dosage Forms

- Reduction in frequency of dosing
- Reduction in overall healthcare costs.
- **Sustained blood levels**
The size and frequency of dosing is determined by the pharmacodynamic and pharmacokinetic properties of the drug. The slower the rate of absorption, the less the blood concentrations fluctuate within a dosing interval. This enables higher doses to be given less frequently. For drugs with relatively short half-lives, the use of extended-release products may maintain therapeutic concentrations over prolonged periods.
- **Attenuation of adverse effects**
With conventional dosage forms, high peak blood concentrations may be reached soon after administration with possible adverse effects related to the transiently high concentration. An example is hypotension in patients taking rapid-release nifedipine products. The use of an extended-release product avoids the high initial blood concentrations which cause the sudden reduction in blood pressure and other significant haemodynamic changes such as

reflex tachycardia. Another example is the transient nausea at sub-toxic concentrations which results from the local irritation caused by high intestinal concentrations of some conventional-release products such as theophylline.

- **Improved patient compliance**
Drugs with short half-lives often need to be given at frequent intervals to maintain blood concentrations within the therapeutic range. There is an inverse correlation between the frequency of dosing and patient compliance. A reduction in the number of daily doses offered by extended-release products has the potential to improve compliance. However, this advantage probably only occurs when conventional formulations need to be given 3 or more times a day^{5,6,7}.

Drug Candidates for Extended-release Products

To be a successful extended-release product, the drug must be released from the dosage form at a predetermined rate, dissolved in the gastrointestinal fluids, maintained at sufficient gastrointestinal residence time, and be absorbed at a rate that will replace the amount of drug being metabolized and excreted.

In general, the drugs best suited for incorporation into an extended-release product have the following characteristics.

- They exhibit neither very slow nor very fast rates of absorption and excretion. Drugs with slow rates of absorption and excretion are usually inherently long-acting, and it is not necessary to prepare them in extended-release forms. Drugs with very short half-lives, that is, less than 2 hours, are poor candidates for extended release because of the large quantities of drug required for such a formulation. Also, drugs that act by affecting enzyme systems may be longer acting than indicated by their quantitative half-lives because of residual effects and recovery of the diminished biosystem.
- They are uniformly absorbed from the gastrointestinal tract. Drugs prepared in

extended-release forms must have good aqueous solubility and maintain adequate residence time in the gastrointestinal tract. Drugs absorbed poorly or at varying and unpredictable rates are not good candidates for extended-release products.

- They are administered in relatively small doses. Drugs with large single doses frequently are not suitable for extended release because the tablet or capsule needed to maintain a sustained therapeutic blood level of the drug would be too large for the patient to swallow easily.
- They possess a good margin of safety. The most widely used measure of the margin of a drug's safety is its therapeutic index, that is, the median toxic dose divided by the median effective dose. For very potent drugs, the therapeutic index may be narrow or very small. The larger the therapeutic index, the safer the drug. Drugs that are administered in very small doses or possess very narrow therapeutic indices are poor candidates for formulation into extended-release formulations because of technologic limitations of precise control over release rates and the risk of dose dumping due to a product defect. Patient misuse (e.g., chewing dosage unit) also could result in toxic drug levels.
- They are used in the treatment of chronic rather than acute conditions. Drugs for acute conditions require greater adjustment of the dosage by the physician than that provided by extended-release products⁸.

Examples of drugs:

- The drug binds to the tissues e.g. tissue-bound ACE inhibitors. For these drugs, less frequent dosing is needed even though the drug may have a short half-life
- The drugs have irreversible effects e.g. the inhibition of platelet cyclo-oxygenase by aspirin
- The relationship between response and plasma/blood concentrations is relatively flat

or if the dose given results in concentrations which are in the plateau region of the dose-response relationship e.g. thiazides in hypertension

- The drug is metabolised to pharmacologically active metabolite(s) which are more slowly cleared than the parent drug e.g. quinapril, trandolapril, venlafaxine⁷.

Extended-release Technology for Oral Dosage Forms

For orally administered dosage forms, extended drug action is achieved by affecting the rate at which the drug is released from the dosage form and/or by slowing the transit time of the dosage form through the gastrointestinal tract.

The rate of drug release from solid dosage forms may be modified by the technologies described next, which in general are based on (a) modifying drug dissolution by controlling access of biologic fluids to the drug through the use of barrier coatings; (b) controlling drug diffusion rates from dosage forms; and (c) chemical reaction or interaction between the drug substance or its pharmaceutical barrier and site-specific biologic fluids.

Coated Beads, Granules, and Microspheres

In these systems, the drug is distributed onto beads, pellets, granules, or other particulate systems. Using conventional pan coating or air suspension coating, a solution of the drug substance is placed on small inert nonpareil seeds or beads made of sugar and starch or on microcrystalline cellulose spheres. The nonpareil seeds are most often in the range of 425 to 850 μm , whereas the microcrystalline cellulose spheres range from 170 to 600 μm . The microcrystalline spheres are considered more durable during production than sugar-based cores.

If the dose of the drug is large, the starting granules of material may be composed of the drug itself. Some of these granules may remain uncoated to provide immediate drug release. Other granules (about two thirds to three fourths) receive varying coats of a lipid material

like beeswax, carnauba wax, glyceryl monostearate, or cetyl alcohol or a cellulosic material like ethylcellulose. Then, granules of different coating thicknesses are blended to achieve a mix having the desired drug-release characteristics. The coating material may be colored to distinguish granules or beads of different coating thicknesses (by depth of color) and to provide distinctiveness to the product. When properly blended, the granules may be placed in capsules or formed into tablets. Various commercial aqueous coating systems use ethylcellulose and plasticizer as the coating material (e.g., Aquacoat [FMC Corporation] and Surelease [Colorcon]). Aqueous coating systems eliminate the hazards and environmental concerns associated with organic solvent-based systems.

The variation in the thickness of the coats and in the type of coating material used affects the rate at which body fluids penetrate the coating to dissolve the drug. Naturally, the thicker the coat, the more resistant to penetration and the more delayed will be drug release and dissolution. Typically, the coated beads are about 1 mm in diameter. They are combined to have three or four release groups among the more than 100 beads contained in the dosing unit. This provides the different desired rates of sustained or extended release and the targeting of the coated beads to the desired segments of the gastrointestinal tract.

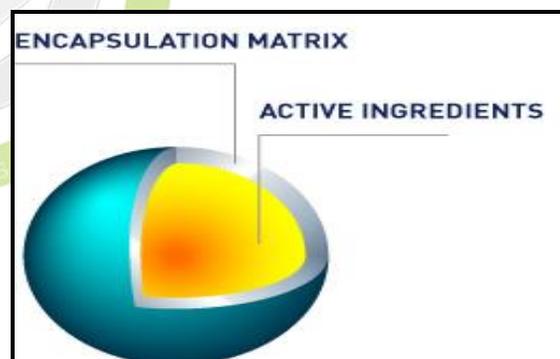
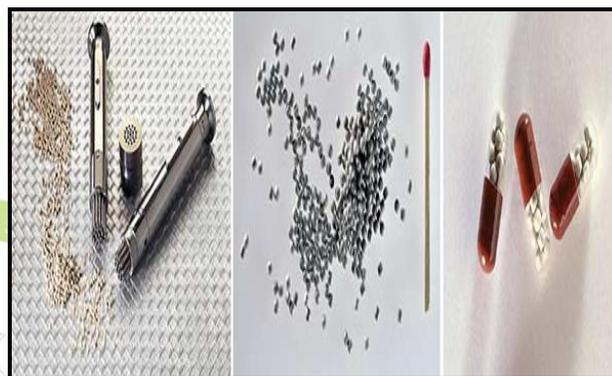
Multi-tablet System

Small spheroid compressed tablets 3 to 4 mm in diameter may be prepared to have varying drug release characteristics. They then may be placed in gelatin capsule shells to provide the desired pattern of drug release. Each capsule may contain 8 to 10 minitables, some uncoated for immediate release and others coated for extended drug release.

Microencapsulated Drug

Microencapsulation is a process by which solids, liquids, or even gases may be enclosed in microscopic particles by formation of thin coatings of wall material around the substance.

The process had its origin in the late 1930s as a cleaner substitute for carbon paper and carbon ribbons as sought by the business machines industry. The ultimate development in the 1950s of reproduction paper and ribbons that contained dyes in tiny gelatin capsules released on impact by a typewriter key or the pressure of a pen or pencil was the stimulus for the development of a host of microencapsulated materials, including drugs. Gelatin is a common wall-forming material, and synthetic polymers, such as polyvinyl alcohol, ethylcellulose, polyvinyl chloride, and other materials also may be used.



The typical encapsulation process usually begins with dissolving the wall material, say gelatin, in water. The material to be encapsulated is added and the two-phase mixture thoroughly stirred. With the material to be encapsulated broken up to the desired particle size, a solution of a second material, usually acacia, is added. This additive material concentrates the gelatin (polymer) into tiny liquid droplets. These droplets (the *coacervate*) form a film or coat around the particles of the substance to be encapsulated as a consequence

of the extremely low interfacial tension of the residual water or solvent in the wall material so that a continuous tight film coating remains on the particle. The final dry microcapsules are free-flowing discrete particles of coated material. The wall material usually constitutes 2% to 20% of the total particle weight. Different rates of drug release may be obtained by changing the ratio of core to wall, the polymer used for the coating, and the method of microencapsulation.

One of the advantages of microencapsulation is that the administered dose of a drug is subdivided into small units that are spread over a large area of the gastrointestinal tract, which may enhance absorption by diminishing local drug concentration. An example of a drug commercially available in a microencapsulated extended-release dosage form is potassium chloride (Micro-K Extencaps, A.H. Robins).

Embedding Drug in Slowly Eroding or Hydrophilic Matrix System

The drug substance is combined and made into granules with an excipient material that slowly erodes in body fluids, progressively releasing the drug for absorption. When these granules are mixed with granules of drug prepared without the excipient, the uncombined granules provide the immediate effect, and the drug-excipient granules provide extended action. The granule mix may be formulated as tablets or capsules for oral delivery.

Hydrophilic cellulose polymers are commonly used as the excipient base in tablet matrix systems. The effectiveness of these hydrophilic matrix systems is based on the successive processes of hydration of the cellulosic polymer, gel formation on the polymer's surface, tablet erosion, and the subsequent and continuous release of drug. Hydroxypropyl methylcellulose (HPMC), a free-flowing powder, is commonly used to provide the hydrophilic matrix. Tablets are prepared by thoroughly distributing HPMC in the formulation, preparing the granules by wet granulation or roller compaction, and manufacturing the tablets by compression.

After ingestion, the tablet is wetted by gastric fluid and the polymer begins to hydrate. A gel layer forms around surface of the tablet, and an initial quantity of drug is exposed and released. As water permeates further into the tablet, the thickness of the gel layer increases and soluble drug diffuses through the gel layer. As the outer layer becomes fully hydrated, it erodes from the tablet core. If the drug is insoluble, it is released as such with the eroding gel layer. Thus, the rate of drug release is controlled by diffusion and tablet erosion.

For a successful hydrophilic matrix system, the polymer must form a gelatinous layer rapidly enough to protect the inner core of the tablet from disintegrating too rapidly after ingestion. As the proportion of polymer in a formulation increases, so does the viscosity of the gel, with a resultant decrease in the rate of drug diffusion and drug release. In general, 20% of HPMC results in satisfactory rates of release for an extended-release tablet formulation. However, as with all formulations, consideration must be given to the possible effects of other formulation ingredients, including fillers, tablet binders, and disintegrants. An example of a proprietary product using a hydrophilic matrix base of HPMC for extended drug release is Oramorph SR Tablets (All Pharma), which contains morphine sulfate.

When hydrophilic matrix formulations are used in the preparation of extended-release capsules, the same concept applies. When the capsule is ingested, water penetrates the capsule shell, comes in contact with the fill, hydrates the outer layer of powder, and forms a gelatinous plug from which the drug content diffuses gradually over time as hydration continues and the gelatinous plug dissolves.

Manufacturers may prepare two-layer tablets, with one layer containing the uncombined drug for immediate release and the other layer having the drug embedded in a hydrophilic matrix for extended release. Three-layer tablets may be similarly prepared, with both outer layers containing the drug for immediate release. Some commercial tablets are prepared with an inner

core containing the extended-release portion of drug and an outer shell enclosing the core and containing drug for immediate release.

Embedding Drug in Inert Plastic Matrix

The drug is granulated with an inert plastic material such as polyethylene, polyvinyl acetate, or polymethacrylate, and the granulation is compressed into tablets. The drug is slowly released from the inert plastic matrix by diffusion.

The compression creates the matrix or plastic form that retains its shape during leaching of the drug and during its passage through the alimentary tract. An immediate-release portion of drug may be compressed onto the surface of the tablet. The inert tablet matrix, expended of drug, is excreted with the feces. The primary example of a dosage form of this type is the Gradumet (Abbott).

Complex Formation

Some drug substances, when chemically combined with certain other chemical agents, form complexes that may be only slowly soluble in body fluids, depending on the pH of the environment. This slow dissolution rate provides the extended release of the drug. Salts of tannic acid, tannates, provide this quality in a variety of proprietary products by the trade name Rynatan (Wallace)¹⁰.

Ion Exchange Resins

A solution of a cationic drug may be passed through a column containing an ion exchange resin, forming a complex by the replacement of hydrogen atoms. The resin–drug complex is washed and may be tableted, encapsulated, or suspended in an aqueous vehicle. The release of the drug depends on the pH and electrolyte concentration in the gastrointestinal tract. Release is greater in the acidity of the stomach than in the less acidic environment of the small intestine. Examples of drug products of this type include hydrocodone polistirex and chlorpheniramine polistirex suspension (Tussionex Pennkinetic Extended Release Suspension [CellTech]) and phentermine resin capsules (Ionamin Capsules [CellTech]).

The mechanism of action of drug release from ion exchange resins may be depicted as follows:

In the Stomach

1. Drug resinate + HCl \rightleftharpoons acidic resin + drug hydrochloride
2. Resin Salt + HCl \rightleftharpoons resin chloride + acidic drug

In the Intestine

1. Drug resinate + NaCl \rightleftharpoons sodium resinate + drug hydrochloride
2. Resin Salt + NaCl \rightleftharpoons resin chloride + sodium salt of drug

This system incorporates a polymer barrier coating and bead technology in addition to the ion exchange mechanism. The initial dose comes from an uncoated portion and the remainder from the coated beads. The coating does not dissolve, and release is extended over 12 hours by ionic exchange. The drug-containing polymer particles are minute and may be suspended to produce a liquid with extended-release characteristics as well as solid dosage forms^{3,8}.

Kinetics of Drug Release

- Drug release from conventional dosage forms, like the other processes of ADME, are governed by the first-order kinetics model.
- In First-order model, drug release is dependent on the amount of drug available for release and therefore *the rate of release declines exponentially with time*.
- Extended release dosage forms are governed by zero-order kinetics in which *the rate of release is independent of amount of drug remaining in the dosage form*.
- Therefore a constant amount of drug will be released over time from extended release dosage forms³.

Therapeutic Limitations of Extended Release Dosage Form

- High cost of preparation.

➤ Reduced potential for dose change or withdrawal in events of toxicity, allergy, or poisoning.

➤ **Dose dumping**

Dose dumping is a phenomenon where by relatively large quantities of drug in a sustained release formulation is rapidly released, introducing potential toxic quantities of the drug into the systemic circulation. Dose dumping can lead to fatalities in case of potent drug, which have a narrow therapeutic index.

➤ **Limited choice of selecting desired dose in the unit**

In conventional dosage forms, dose adjustments are much simpler e.g. tablet can be divided into two fractions. In case of sustained release dosage forms, this appears to be much more complicated. Sustained release property may get lost, if dosage form is fractured.

➤ **Poor *In vitro* – *In vivo* correlation**

In sustained release dosage form, the rate of drug release is deliberately reduced to achieve drug release possibly over a large region of gastrointestinal tract. Here the so called ‘Absorption window’ becomes important and may give rise to unsatisfactory drug absorption *In vivo* despite excellent *In vitro* release characteristics.

➤ **Patient variation**

The time period required for absorption of drug released from the dosage form may vary among individuals. Co-administration of other drugs, presence or absence of food and residence time in gastrointestinal tract is different among patients. This also gives rise to variation in clinical response among the patient⁹.

Designing Extended-release Drug Delivery System

The oral route of administration is the most preferred route due to flexibility in dosage form, design and patient compliance. But here one has to take into consideration, the various pH that the dosage form would encounter during its transit, the gastrointestinal motility, the enzyme

system and its influence on the drug and the dosage form. The majority of oral sustained release systems rely on dissolution, diffusion or a combination of both mechanisms, to generate slow release of drug to the gastrointestinal milieu. Extended (zero-order) drug release has been attempted to be achieved by following classes^{4,10}.

A) Dissolution Controlled Release Systems

Dissolution-controlled release can be obtained by slowing the dissolution rate of a drug in the GI medium, incorporating the drug in an insoluble polymer and coating drug particles or granules with polymeric materials of varying thickness.

The rate of dissolution (dm/dt) can be approximated by following equation:

$$\frac{dm}{dt} = \frac{ADS}{h}$$

Where,

A = Surface area of the dissolving particle or tablet

D = Diffusivity of the drug

S = Aqueous solubility of the drug

h = Thickness of the boundary layer

It is further divided into reservoir type and matrix type dissolution controlled release systems.

➤ **Reservoir type dissolution controlled release system**

In this type, the drug particles are coated or encapsulated by one of the several microencapsulation techniques with slowly dissolving materials like cellulose and polyethylene glycol.

➤ **Matrix type dissolution controlled release system**

In this type drug is homogeneously dispersed throughout the rate controlling medium, this system is also called as monolith system. It is very common and employ waxes such as beeswax, carnauba wax which control the drug

release rate by controlling the rate of dissolution fluid penetration into the matrix by altering the porosity of tablet, decreasing its wettability or by itself getting dissolved at a slower rate.

B) Diffusion Controlled Release Systems

In this type of systems, the diffusion of dissolved drug through a polymeric barrier is a rate limiting step. Diffusion of a drug molecule through a polymeric membrane forms the basis of these controlled drug delivery systems. It is also further divided into 2 types as follows:

➤ Reservoir devices (Laminated matrix devices)

These systems are hollow containing an inner core of the drug surrounded in the water insoluble polymer membrane. The polymer can be applied by coating or microencapsulation techniques. The drug release mechanism across the membrane involves its partitioning into the membrane with subsequent release into the surrounding fluid by diffusion.

➤ Matrix devices

In this type, the drug is dispersed in an insoluble matrix of rigid, non-swellable hydrophobic material or swellable hydrophilic substances and the drug release is dependent on rate of drug diffusion and not on solid dissolution rate.

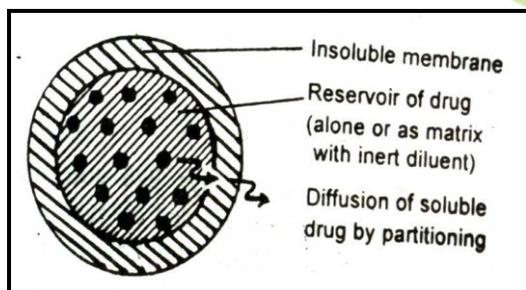


Figure 1.2 Reservoir system

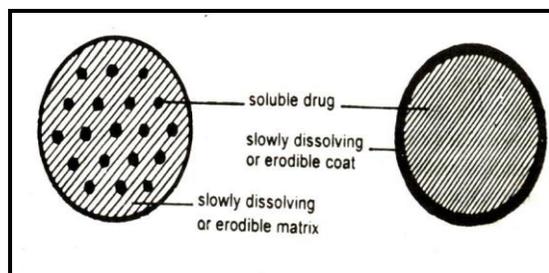


Figure 1.3 Matrix system

In the case of a reservoir type diffusion controlled device, the rate of drug released (dm/dt) can be calculated using the following equation:

$$\frac{dm}{dt} = \frac{ADK}{L} \Delta c$$

Where,

A = Area

D = Diffusion coefficient

K = Partition coefficient of the drug between the drug

core and the membrane

L = Diffusion path length and

C = Concentration difference across the membrane

C) Diffusion and dissolution controlled release systems

In such systems, the drug core is encased in a partially soluble membrane. Pores are thus created due to dissolution of parts of the membrane which permit entry of aqueous medium into the core and hence drug dissolution and allow diffusion of dissolved drug out of the system^{11,12}.

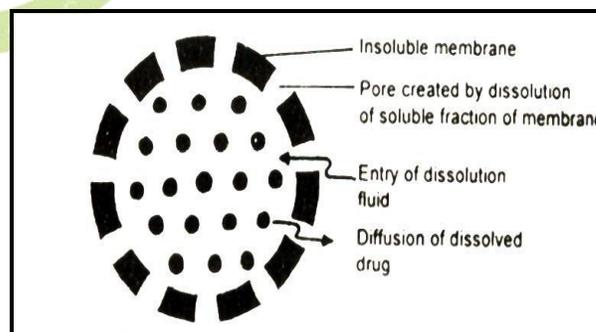


Fig.1.4 Dissolution and diffusion controlled release system

Polymers Used in Matrix Tablets

There are number of polymers which may be used to formulate matrix tablets depending on the physicochemical properties of the drug substance to be incorporated into matrix system and type of drug release required. Polymers used for matrix tablets may be classified as^{13,14}

A) Hydrogels:

- Poly-hydroxyethyl methacrylate (PHEMA)
- Cross-linked polyvinyl alcohol (PVA)
- Cross-linked Polyvinyl pyrrolidone (PVP)
- Polyethylene oxide (PEO)
- Polyacrylamide (PA)

B) Soluble polymers:

- Polyethylene glycol (PEG)
- Polyvinyl alcohol (PVA)
- Polyvinyl pyrrolidone (PVP)
- Hydroxypropyl methyl cellulose (HPMC)

C) Biodegradable polymers:

- Polylactic acid (PLA)
- Polyglycolic acid (PGA)
- Polycaprolactone (PCL)
- Polyanhydrides
- Polyorthoesters

D) Non-biodegradable polymers:

- Polyethylene vinyl acetate (PVA)
- Polydimethyl siloxane (PDS)
- Polyether urethane (PEU)
- Polyvinyl chloride (PVC)
- Cellulose acetate (CA)
- Ethyl cellulose (EC)

E) Mucoadhesive polymers:

- Polycarbophil,
- Sodium Carboxymethyl cellulose
- Polyacrylic acid
- Tragacanth
- Methyl cellulose
- Pectin

F) Natural gums:

- Xanthan gum
- Guar gum
- Karaya gum
- Gum Arabic
- Locust bean gum

Commercial examples:

- Toprol-XL[®] (metoprolol succinate) tabs. (Astra);
- Indocin SR[®] (indomethacin capsules (Merck);
- Compazine[®] (prochlorperazine) Spansule Capsules (SmithKline Beecham)

Evaluation

Weight Variation

Weight variation was calculated as per method described in Indian Pharmacopoeia (I.P. 2007). 20 tablets are weight individually by using Electronic balance and the average weight is calculated. The requirements are met if the weights of not more than 2 of tablets differ by more than the percentage listed in table 8.9 and no tablets differ in weight by more than double that percentage.

Limits for weight variation in tablet

Average weight of tablet in mg (I.P. 2007)	Average weight of tablet in mg (USP32)	Percentage deviation allowed
80 mg or less	120 mg or less	±10
In between 80 mg - 250 mg	In between 120mg - 324mg	±7.5
250 mg or more	325mg or more	±5

Thickness

Thickness of tablet is important for uniformity of tablet size. Thickness is measure using Vernier Calipers.

Hardness

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet is checked by using sclenger hardness tester. The hardness is measure in terms N/cm².

Friability (IP2007)

Friability is the measure of tablet strength. Roche friabilator (Lab India) is used for testing the friability using the following procedure: tablet weight equivalent to 6.5mg or minimum 10 tablets are weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of 6 inches with each revolution. After 100 rotations the tablets were weighed and the percentage loss in tablet weight is determined.

Following formula is used to calculate the friability

$$\%F = 1 - (\text{loss in weight} / \text{initial weight}) \times 100$$

CONCLUSION

From the above discussion, it concludes that the extended release dosage form are drug delivery system which by virtue of formulation and product design, provide drug release in a modified form distinct from that of the conventional dosage forms. Drug release can either be delayed or extended in nature. It is effective tool for drugs that are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic effects; when compared to conventional dosage form it provides improved patient compliance. This concept, however, requires accurate adjustment of the physicochemical parameters of core material, coating formulation and tableting excipients. Many drugs are formulated as extended release dosage form to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of

time after administration of single dose of drug. Hence, extended release drug delivery system is the preferred dosage form for the drugs having short half-life, so as to maintain the drug plasma level in therapeutic index for prolonged period of time.

REFERENCES

1. *Novel Drug Delivery System (NDDS)*. K. Senthil Kumar. M.Pharm Asst. professor Department of Pharmaceutics QIS college of pharmacy Ongole, A.P-India 4/18/2011.
2. Mamidala, R. K., Ramana, V., Lingam, M., Gannu, R., Yamsani, M. R. (2009). Factors influencing the design and performance of oral sustained/controlled release dosage forms. *Int. J. Pharm. Sci. Nanotechnol.*, 2(3), 583-594.
3. *Modified Release Dosage Forms*. A. S. Adebayo Phd,
4. Modi, S. A., Gaikwad, P. D., Bankar, V. H., Pawar, S. P. (2012). Sustained release drug delivery system: a review. *Int. J. Pharma Res. Dev.*, 2(12), 147-159.
5. Opie LH, Messerli FH. (1995). Nifedipine and mortality: grave defects in the dossier. *Circulation*, 92, 1068-73.
6. Schall, R., Müller, F. R., Müller, F. O., & Luus, H. G. (1997). Bioequivalence of controlled-release calcium antagonists. *Clinical Pharmacokinetics*, 32(1), 75-89.
7. Sansom, L. N. (1999). Oral extended-release products. *Australian prescriber*, 22, 88-90.
8. Ansel, H. C., Popovich, N. G., & Allen, L. V. (1990). *Pharmaceutical dosage forms and drug delivery systems* (p. 106). Philadelphia: Lea & Febiger.
9. Jayanthi, B., Manna, P. K., Madhusudhan, S. K., Mohanta, G. P., Manavalan, R. (2011). Per oral extended release products - An overview. *J. Apl. Pharm. Sci.*, 1(2), 50-55.
10. Sampath, K. K., Debjit, B., & Tripath, K. K. (2010). Innovations in sustained release drug

- delivery system and its market opportunities. *Journal of Chemical and Pharmaceutical Research, J. Chem. Pharm. Res.*, 2(1), 349-360.
11. <http://www.iptonline.com/articles/public/IPTTWELVE80NoPrint.pdf>, accessed on November, 2011.
 12. http://shodhganga.inflibnet.ac.in/bitstream/10603/2188/12/12_chapter%203.pdf 10, accessed on November, 2011.
 13. Dash, T. R., & Verma, P. (2013). Matrix tablets: an approach towards oral extended release drug delivery. *International Journal of Pharma Research & Review*, 2(2), 12-24.
 14. Patel, H., Panchal, D. R., Patel, U., Brahmabhatt, T., & Suthar, M. (2011). Matrix type drug delivery system: A review. *Journal of Pharmaceutical Sciences and Bioscientific Research*, 1(3), 143-151.

